REMARKS

Applicant has carefully reviewed and considered the Office Action mailed on July 2, 2003, and the references cited therewith.

Claim 1 is amended, and claims 2 and 10-34 are canceled; as a result, claims 1 and 3-9 are now pending in this application.

Interview Summary

Applicant thanks Examiner Winkler for the courtesies extended to Applicants and Applicants' Representative during the interview of August 27, 2003 and August 29, 2003. Issues relating to the rejection under 35 U.S.C. § 112, second paragraph, were discussed, including proposed experiments and possible claim amendments.

Rejection of the Claims Under 35 U.S.C. § 112, Second Paragraph

The examiner has maintained the rejection of Claims 1-9 under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. In particular, the examiner states that applicant's "own disclosure in the specification on page 26, lines 10-13 [states that] 'the Dh-OLF isolated herein at fraction 27.5 showed an identical chromatographic retention to the standard component dho-B.'" Claim 2 has been cancelled. Insofar as this rejection is applied to the pending claims 1 and 3-9, it is hereby traversed.

The examiner is invited to note that the statement at page 26, lines 10-13 of the specification indicates that under certain experimental conditions Dh-OLF and dho-B have similar chromatographic retention values. Under more stringent experimental conditions, however, it becomes evident that Dh-OLF and dho-B, are in fact, different compounds. The Examiner's attention is drawn to the Supplemental Declaration of Dr. Valdes ("Supplemental Declaration"), which provides experimental evidence that Dh-OLF and dho-B are different compounds. In this Supplemental Declaration Dr. Valdes states that physical properties related

to molecular polarity and solubility of lactone hydrogenated ouabain-like factor (Dh-OLF) isolated from different mammalian sources can be distinguished by HPLC analysis.

First, experiments were performed to verify that human serum Dh-OLF and bovine adrenal Dh-OLF co-migrated chromatographically. In these experiments purified Dh-OLF from humans serum and from bovine adrenal cortex were mixed together and co-injected on HPLC using an isocratic 10% CH_3CN mobile phase. The two molecules showed a single band of elution time of 26 minutes (**Figure 1 of Supplemental Declaration**). This same HPLC technique has previously been demonstrated to separate Dh-OLFs with fine structural resolution. Thus, co-migration using these techniques is consistent with material from these two distinct mammalian sources being similar compounds.

Second, experiments were performed to verify that chromatographically mammalian Dh-OLF separates differently from plant-derived dho compounds. Pure human serum Dh-OLF and bovine adrenal cortex Dh-OLF (Qazzaz et al., Endocrinology, 2000;141(9):3200-3209) and their plant related counterpart Dihydroouabain-isomer B (pure Dho-B obtained from HPLC separation of dihydroouabain commercial preparation, Qazzaz et al., Biochem Biophys Acta, 1999:1472:486-497) were mixed together and co-injected on HPLC using an isocratic 10% CH_3CN mobile phase. The three molecules showed two bands separated by a minimum of 1 minute (**Figure 2 of Supplemental Declaration**). The first band (26 min) was identified (see above) as a co-eluting mixture of the two sources of Dh-OLF (human serum and adrenal cortex, *see* **Figure 1 of Supplemental Declaration**) and the second band eluted at 28 min representing dho-B. Similarly, the genin compounds (aglycone without the sugar molecules) of both parents (human serum Dh-OLF and Dho-B) when mixed and injected on HPLC also clearly separated by 1 to 1.5 minutes using the same isocratic HPLC mode. While the parent compounds, human serum Dh-OLF and Dho-B eluted at 26 and 28 respectively those of their genin components (human serum Dh-OLF-genin and dihydroouabain-B-genin) eluted at 18 and 20 minutes respectively (**Figure 3 of Supplemental Declaration**). This demonstrates conclusively that mammalian-derived Dh-OLF is chromatographically distinct from plant-derived dihydroouabain.

In summary, two important findings are detailed in the Supplemental Declaration: 1) Dh-OLF isolated from human serum does not separate from Dh-OLF isolated from bovine adrenal glands; and 2) Dh-OLF isolated from human serum chromatographically separates from the plant-derived dihydroouabain isomer B (dho-B). These data demonstrate that Dh-OLF extracted form human serum is similar to that extracted from bovine adrenal glands and that Dihydro-OLF is different from the plant-related counterpart, dihydroouabain (dho-B).

Thus, Applicant requests that the rejection of claims 1 and 3-9 under 35 U.S.C. § 112, second paragraph be withdrawn.

§102 Rejection of the Claims

Claims 1-9 were rejected under 35 U.S.C. § 102(b) as being anticipated by Klaus Repenning (U.S. 3,113,128). Also, claims 1-9 were rejected under 35 U.S.C. § 102(b) as being anticipated by Qazzas et al. (Abstract FASEB Journal 1997). Claim 2 has been cancelled. Insofar as these rejections are applied to the pending claims 1 and 3-9, they are hereby traversed.

In particular, the Examiner indicates that dho-B from a plant source is the same as the Dh-OLF derived from a mammalian source. As discussed in detail above, under certain experimental conditions Dh-OLF and dho-B have similar chromatographic retention values, but that under more stringent experimental conditions, Dh-OLF and dho-B, in fact, have different chromatographic retention values, indicating that mammalian-derived Dh-OLF and plant-derived dho-B are indeed different compounds. Thus, the compounds as recited by the present claims are distinguishable over the cited art.

Applicant requests that the rejections of claims 1 and 3-9 under 35 U.S.C. § 102(b) be withdrawn.

CONCLUSION

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (612) 373-6961 to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Mail Stop AF, Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 2nd day of December, 2003

Gina M. Uphus _____
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